REMARKS

Status of the Claims

Claims 1-25 are pending in the application. Claims 13-15 and 20-15 have been withdrawn as drawn to a non-elected invention. Claims 1-12 and 16-19 are currently under examination.

Claim Amendments

Claim 1 has been amended to recite the full name of MELK and the full name of RAC and to clarify that a test agent is identified as a candidate RAC pathway modulating agent by determining the activity or expression of the MELK polypeptide or nucleic acid in the assay system in the presence or absence of the test agent. Support for the amendment is found throughout the specification, and particularly at, for example pages 2, 3, and 19-30.

Claim 10 has been amended to recite the full name for PMO. Support for the amendment is found at page 18.

Claim 11 has been amended to clarify that detecting a phenotypic change in the model system indicates that the RAC function is restored when compared relative to wild-type cells. Support for the amendment is found throughout the specification, for example at pages 23, 25, and 26.

Claim 16 has been amended to clarify that the second assay is capable of detecting a change in the RAC pathway and that confirmation of the test agent as a candidate RAc pathway modulating agent is achieved by measuring the RAC pathway in the presence or absence of the test agent. Support for the amendment is found throughout the specification, and particularly at, for example pages 2, 3, and 19-32.

Claims 17 and 18 have been amended merely to provide proper antecedent basis.

Amendments to the claims are made without prejudice and do not constitute amendments to overcome any prior art or other statutory rejections. Additionally, these amendments are not an admission regarding the patentability

of subject matter of the amended claims and should not be so construed. Applicant reserves the right to pursue the subject matter of the previously filed claims in this or in any other appropriate patent application.

Claim Objections

The Office objected to claims 1, 10, and 16 because the claims do not recite the full name of RAC and MELK. Claim 1 has been amended to include recitation of the full name for MELK, ie, Maternal Embryonic Leucine Zipper Kinase and the full name for RAC, i.e., RAS-related C3 botulinum toxin substrate. Applicant respectfully requests withdrawal of this objection to the claims.

The Office objected to claim 10 because the claim does not recite the full name of PMO. Claim 10 has been amended to include recitation of the full name for PMO, ie, phosphothioate morpholino oligomer. Applicants respectfully request withdrawal of this objection to claim 10.

The Office objected to the wording of step (b) in claim 1 and the wording of step (e) in claim 16. Claims 1 and 16 have been amended to correct the wording in accordance with the Office's suggestion. Applicants respectfully request withdrawal of this objection to claims 1 and 16.

35 U.S.C. § 112, First Paragraph, Rejections

Enablement

Claims 1-12 and 16-19 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement because the claim(s) contains subject matter that was not described in the specification in such a way so as to enable one skilled in the art to which it pertains, or with which it is most closely connected, to make and/or use the invention. The Applicants respectfully traverse these rejections.

The Examiner alleged that the claims are not enabled because he "could not find concrete scientific evidence that MELK is involved in the RAC pathway". The Examiner considered the expression data provided in the specification and stated that "Applicants have not shown any data [linking] the MELK with RAC

pathway". The Office asserted that the instant specification "assumes" that MELK plays a role in the RAC pathway and thus any agent capable of modulating MELK can be potentially called a RAC modulator. Thus, the Office concluded that the claims are not enabled because it would require further investigation to verify whether MELK is involved in the RAC pathway.

The test of enablement is whether one reasonably skilled in the art (1) could make and use the invention (2) from the disclosures in the application coupled with information known in the art (3) without undue experimentation. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988); *United States v. Telectronics, Inc.*, 857 F.2d 778 (Fed. Cir. 1988); M.P.E.P. § 2164.01. Thus, under 35 U. S. C. § 112, all that is required is that the specification describe the invention in such terms as to enable a person skilled in the art to make and use the invention.

Contrary to the Office's allegation, the specification clearly teaches one skilled in the art how to make and use the claimed assay for identifying a candidate RAC pathway modulating agent. First, the specification describes the function and structure of the MELK polypeptide and further provides several MELK polypeptide and nucleic acid sequences that can be used in the screening assays at pages 4-7. In addition, the specification clearly provides numerous examples of assays using the described MELK polypeptides and nucleic acids that can be employed to identify a candidate RAC pathway modulating agent. (Specification at pages 19-30). Furthermore, the specification provides numerous examples of assays that can be used to confirm that the identified agent is a RAC pathway modulating agent. (Specification at 30-32). Applicant submits that performing the assays described in the specification is within the skill of the ordinary artisan.

The Office alleged that the claimed assays are not enabled because there is no data linking MELK with the RAC pathway and therefore further investigation is required to verify whether MELK is involved in the RAC pathway. Contrary to the Office's contention, the specification provides data linking MELK with the RAC pathway. Initially, the specification teaches that *ced-10*, *mig-2*, and *rac-2* encode RAC-related proteins and that these genes function to control a number

of cell and axonal migrations in *C.elegans*. The specification further teaches that inactivation of two or three of these genes causes significant migration defects, whereas mutation in only one of these genes does not. Specifically, the specification teaches that *ced-10*/*mig-2* double mutants have gross morphological and movement defects not seen in either single mutant and that the phenotype of the *ced-10*/*mig-2* double mutant includes slow growth, and vulval, withered tail, and sterility defects, none of which is seen with either single mutant (specification at pages 1, and 34-35). Thus, *ced-10* and *mig-2* single mutants resemble wildtype worms in morphology and movement, whereas *ced-10*/*mig-2* double mutants have strong morphological and movement defects.

The link between MELK and the RAC pathway was determined using two separate assays involving *C.elegans* in which a specific gene was inactivated by RNAi. The assay methods and results are described in the specification at pages 4 and 34-35. Herein, the Applicants describe a first assay in which wildtype *C.elegans*, single *ced-10* mutants, and single *mig-2* mutants, each having the same specific gene inactivated by RNAi were observed for morphological and movement defects resembling those of the *ced-10*/*mig-2* double mutants.

Those genes that, when inactivated, result in a worm with a double *ced-10*/*mig-2* mutant phenotype in the single *ced-10* or single *mig-2* mutant *C.elegans* and not in the wildtype *C.elegans* were furthered studied in a second direct cell migration assay. The direct cell migration assay measures the migration of a subset of mechanosensory neurons (AVM and ALM) in *C.elegans* larvae. Those larvae having the *ced-10/mig-2* double mutation show short or misguided AVM and ALM migration compared to wildtype larvae or larvae having the single *ced-10* or single *mig-2* mutation.

The migration of AVM and ALM cells in worms subjected to RNAi treatment demonstrating a double *ced-10*/*mig-2* mutant phenotype in single *ced-10* or single *mig-2* mutant *C.elegans* was compared with the migration of AVM and ALM cells in (1) wildtype C.elegans, (2) *C.elegans* single *ced-10* mutants, and (3) *C.elegans* single *mig-2* mutants. Those genes that, when inactivated by RNAi treatment, cause short or misguided migration of AVM and ALM cells (as

compared with wildtype and single mutant *C.elegans*) are relevant to the RAC pathway. One such gene, 4B260, was identified. In other words, inactivation of 4B260 causes short or misguided cell migration in *C.elegans*. The human ortholog of the 4B260 gene is MELK.

One skilled in the art of genetic screening would understand that the two screening assays used and described in the specification are evidence of a link between MELK and the RAC pathway. Specifically, Applicants have shown that inactivation of 4B260/MELK by RNAi results in Rac-associated (i.e., ced-10 or mig-2 associated) changes in neuronal cell migration. Therefore, agents that modulate MELK (inhibit or enhance MELK) can be used to identify candidate RAC pathway modulating agents.

One skilled in the art knows that many tumor cells exhibit altered (typically enhanced) cell migration. As further evidence of MELK's role in a disease associated with altered cell migration, Applicants have shown that various tumor cells have overexpressed MELK compared to tissue-matched normal cells. (specification at pages 37-39).

Applicants submit that the claimed methods are fully enabled for the reasons set forth above. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-12 and 16-19 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement.

Written Description

Claims 1-12 and 16-19 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement because the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Applicants respectively traverse these rejections.

The Office argued that the specification does not satisfy the written description requirement because it fails to show sufficient evidence that MELK is

involved in the RAC pathway and thus it fails to demonstrate that Applicants had possession of the claimed methods.

Under 35 U.S.C. § 112, first paragraph, all that is required to satisfy the written description requirement is that the specification describe the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991); M.P.E.P § 2163(I). Whether the specification shows that an applicant was in possession of the claimed invention is a factual determination. M.P.E.P. § 2163(I). Factors to be considered in determining whether there is sufficient evidence of possession include: (1) the level of skill and knowledge in the art; (2) partial structure; (3) physical and/or chemical properties; (4) functional characteristics alone or coupled with a known or disclosed correlation between structure and function; and (5) the method of making the claimed invention. *Id.* at (II)(A)(2)-(3)(a). Disclosure of <u>*any*</u> combination of such identifying characteristics that distinguish the claimed invention such that one skilled in the art would conclude that the applicant was in possession of the claimed species is sufficient. *Id*; *see Reagents of the Univ. of Calif. v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Contrary to the Office's allegation, the specification fully describes the claimed methods in sufficient detail to show possession of the invention. For example, the specification fully describes the structure and function of MELK polypeptides and nucleic acids at pages 2, and 4-7. In addition, the specification describes in detail numerous examples of assays comprising the MELK polypeptides or nucleic acids that can be used to identify a candidate RAC modulating agent by detecting the activity or expression of the MELK polypeptides or nucleic acids in the presence of the test agent. Specification at pages 19-30. The specification also fully describes second assays that measure a change in the RAC pathway that can be used to confirm the test agent as a RAC modulating agent. Specification at pages 19-32. The specification further

describes exemplary agents that can be tested using the described assays. Specification at pages 12-19.

Despite this detailed description and clear showing of possession of the claimed methods, the Office argued that the specification does not satisfy the written description requirement because it allegedly fails to establish a sufficient link between MELK and the RAC pathway. As discussed previously, the specification provides evidence of a link between MELK and the RAC pathway at pages 4 and 34-35.

For the reasons indicated above, Applicants submit that the specification demonstrates possession of the claimed invention and thereby satisfies the written description requirement. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-12 and 16-19 under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the written description requirement.

CONCLUSION

In view of the foregoing, the applicants respectfully request reconsideration of the pending claims. If it is believed that such contact would expedite prosecution of the present patent application, the Patent Office is urged to contact the undersigned.

Respectfully submitted,

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